EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	3030	gad or (glutamic adj acid adj decarboxylase)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/05/11 13:27
S2	9	S1 and 65kd	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/05/11 13:31
S3	7	"4473495"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/05/11 13:28
S4	3	(("4473495") or ("20020090357")).PN.	USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/05/11 13:29
S5	67	S1 same "65" same iddm	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/05/11 13:32
S6	15	gad65 same cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/05/11 13:32

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Decarboxylase)
  Record Date Created: 20010620
  Record Date Completed: 20010719
?




Set     Items   Description
S1      15631   GAD OR (GLUTAMIC ACID DECARBOXYLASE)
S2     781755   IDDM OR DIABETES
S3       3997   S1 AND S2
S4       1849   S1 AND 65
S5        922   S4 AND S2
S6        455   RD S5  (unique items)
S7        324   S6 NOT PY>=2002
S8        324   RD S7  (unique items)
S9        131   S6 NOT PY<2002
?




Set     Items   Description
S1      15631   GAD OR (GLUTAMIC ACID DECARBOXYLASE)
S2     781755   IDDM OR DIABETES
S3       3997   S1 AND S2
S4       1849   S1 AND 65
S5        922   S4 AND S2
S6        455   RD S5  (unique items)
S7        324   S6 NOT PY>=2002
S8        324   RD S7  (unique items)
S9        131   S6 NOT PY<2002
S10      1849   S1 AND 65
S11       342   S10 AND IDDM
S12       167   RD S11  (unique items)
S13       160   S12 NOT PY>=2002
?
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TYPE S7/FULL/1-10

7/9/1 (Item 1 from file: 154)

DIALOG(R)File 154:MEDLINE(R)
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13552590 PMID: 11894970

Cytotoxic T lymphocyte antigen 4 gene polymorphism confers susceptibility to type 1 diabetes in Japanese children: analysis of association with HLA genotypes and autoantibodies.

Kikuoka N; Sugihara S; Yanagawa T; Ikezaki A; Kim H S; Matsuoka H; Kobayashi Y; Wataki K; Konda S; Sato H; Miyamoto S; Sasaki N; Sakamaki T; Niimi H; Murata M
Department of Pediatrics, Tokyo Women's Medical University, Daini Hospital, Japan.

Clinical endocrinology (England) Nov 2001, 55 (5) p597-603, ISSN 0300-0664--Print Journal Code: 0346653
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

OBJECTIVE: Although the polymorphisms of the cytotoxic T lymphocyte antigen 4 (CTLA4) gene have been shown to be associated with Type 1 diabetes in Caucasians, some conflicting results have been reported among subjects of different ethnic backgrounds. We examined a CTLA4 polymorphism and its relationship to human leucocyte antigen (HLA) genotypes and autoantibodies for glutamic acid decarboxylase 65 (GAD65) and IA-2 in Japanese children with Type 1 diabetes. SUBJECTS AND MEASUREMENTS: The study group consisted of 125 childhood-onset Japanese subjects (50 males, 75 females) with Type 1 diabetes. The CTLA4 A/G polymorphism at position 49 was analysed using a PCR-restriction fragment length polymorphism (PCR-RFLP) method. The HLA-DRB1 and DQB1 genotypes were defined by DNA analysis using PCR-sequence-specific oligonucleotide (PCR-SSO) probes. The GAD65 autoantibody (GAD65Ab) and IA-2 autoantibody (IA-2Ab) titres were measured using radioimmunoassay. RESULTS: The distribution of genotype frequencies differs between subjects with Type 1 diabetes (GG: 46%, AG: 50%, AA: 5%) and controls (GG: 39%, AG: 44%, AA: 17%) ($P < 0.01$). The frequency of the G allele is higher in the diabetes group than in the controls ($P < 0.05$). When the subjects were subdivided according to HLA genotype, the two major HLA high-risk groups, with DR9-DQ9 and DR4-DQ4, that are unique to Japanese populations showed no difference in their CTLA4 polymorphism frequencies. Although no association between the CTLA4 polymorphism and the prevalence of GAD65Ab was found, CTLA4 GG subjects that had been newly diagnosed (< 9 months) had significantly higher levels of autoantibodies than AG subjects ($P < 0.01$). The prevalence and titres of IA-2Ab were not associated with the CTLA4 polymorphism. CONCLUSIONS: The CTLA4 gene might confer a susceptibility to childhood-onset Type 1 diabetes in the Japanese population. The association between this CTLA4 polymorphism and the HLA genotype was similar for both major groups with HLA high-risk alleles. CTLA4 might contribute to the humoral immune response to GAD in newly diagnosed subjects.

Tags: Female; Male
Descriptors: *Antigens, Differentiation--genetics--GE; *Diabetes Mellitus, Type 1--genetics--GE; *Genetic Predisposition to Disease; *Immunoconjugates; *Polymorphism, Genetic; Adolescent; Autoantibodies--blood--BL; Autoantibodies--immunology--IM; Case-Control Studies; Child; Child, Preschool; Diabetes Mellitus, Type 1--immunology--IM; Gene Frequency ; Glutamate Decarboxylase--immunology--IM; HLA Antigens--genetics--GE; HLA-DQ Antigens--genetics--GE; HLA-DR Antigens--genetics--GE; Humans; Infant; Japan; Polymorphism, Restriction Fragment Length; Research Support, Non-U.S. Gov't

CAS Registry No.: 0 (Antigens, Differentiation); 0 (Autoantibodies); 0 (HLA Antigens); 0 (HLA-DQ Antigens); 0 (HLA-DQB1); 0 (HLA-DR Antigens); 0 (ICA512 autoantibody); 0 (Immunoconjugates); 0 (cytotoxic T lymphocyte-associated antigen 4-immunoglobulin); 0 (cytotoxic T-lymphocyte antigen 4); 128338-86-3 (HLA-DRB1 antigen)
Enzyme No.: EC 4.1.1.15 (Glutamate Decarboxylase)
Record Date Created: 20020315
Record Date Completed: 20020326

7/9/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13516872 PMID: 11774856
Secular and seasonal cycling of IA2-ab autoantibody in Slovak diabetic children.
Mikulecky M; Michalkova D
Institute of Preventive and Clinical Medicine, Ist Pediatric Clinic, Children's Teaching Hospital, Comenius Universitv, Bratislava, Slovak Republic. mikuleky@upkm.sk
Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie (France)
2001, 55 Suppl 1 p106s-109s, ISSN 0753-3322--Print Journal Code: 8213295
Publishing Model Print
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

The concept of seasonal and secular cycling of initial autoantibody plasma levels in children with diabetes mellitus 1 is not common, despite the known fluctuations in one of the triggering factors, i.e., various enteroviral infections. The aim of this study was therefore to assess the trends and cycles in the time series of IA2-autoantibody (ab) blood plasma levels measured in each patient at the moment of diagnosis of the disease, before the first injection of insulin. In a retrospective study, the IA2-ab data, with each item related to a calendar day, were analyzed from 83 male and 108 female patients aged up to 14 years, with the date of disease menifestation between January 1993 and December 1999. The data source was the Slovak National Register of Childhood Diabetes. The plasma levels of the autoantibody against pancreatic tyrosine phosphatase (IA2-ab) were measured by radioimmunoassay. The chronogram of the daily observed values, modified by moving averages, from three successive data items per patient, was processed by Halberg's cosinor method to test the presence of seven-year sinusoids and one-year rhythms. One seven-year sinusoid, peaking in February 1998 (boys) and in October 1996 (girls), and a seasonal rhythm culminating in May/June each year were significant. There are some similarities to the cycling of other variables such as the incidence of diabetes, the birth of future diabetics, Coxsackie virus epidemics and pancreatic glutamic acid decarboxylase (GAD 65) autoantibody. Moreover, some cosmo-geophysical periods also seem to be cycling in a parallel manner. The novelty of this contribution is that it examines the seasonal cycling of the autoantibody, connected with the pathogenesis of diabetes and directed against IA2-ab.

Tags: Female; Male
Descriptors: *Autoantibodies--blood--BL; *Diabetes Mellitus--blood--BL; *Diabetes Mellitus--immunology--IM; *Pancreas--immunology--IM; *Protein-Tyrosine-Phosphatase--blood--BL; *Protein-Tyrosine-Phosphatase--immunology--IM; *Seasons; Adolescent; Biological Markers; Child; Child, Preschool; Diabetes Mellitus--epidemiology--EP; Enterovirus--immunology--IM; Humans; Sex Characteristics; Slovakia--epidemiology--EP
CAS Registry No.: 0 (Autoantibodies); 0 (Biological Markers)

Enzyme No.: EC 3.1.3.- (protein tyrosine phosphatase IA-2); EC 3.1.3.48 (Protein-Tyrosine-Phosphatase)
Record Date Created: 20011231
Record Date Completed: 20020612

7/9/3 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13423381 PMID: 11600569
Autoantibodies and human leucocyte antigen class II in first-degree family members of Mexican-American type 1 diabetic patients.
Zeidler A; Raffel L J; Costin G; Shaw S J; Buchanan T A; Noble J; Rotter J I; Palmer J; Krischer J P; Wait C; Maclaren N K
Division of Endocrinology and Diabetes, LAC-USC Medical Center, Keck USC School of Medicine, 1200 North State Street, Los Angeles, CA 90033, USA. azeidler@hsc.usc.edu
Journal of clinical endocrinology and metabolism (United States) Oct 2001, 86 (10) p4957-62, ISSN 0021-972X--Print Journal Code: 0375362
Contract/Grant No.: R01-MD-19467-12; PHS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: AIM; INDEX MEDICUS

As part of a genetic study of type 1 diabetes in Mexican-Americans, 360 first-degree relatives of 108 type 1 diabetic probands were studied. Islet cell antibody (ICA), insulin autoantibody, glutamic acid decarboxylase (GAD(65)), and protein tyrosine phosphatase autoantibodies were measured and human leucocyte antigen (HLA) class II alleles DRB1 and DQB1 genotyping was performed. ICA was positive in 37% of the probands and 5.8% of the relatives. A subgroup of 26 probands (12 ICA+, 14 ICA-) was tested for GAD(65) and was found positive. 4/14 ICA+ first-degree relatives were GAD(65) positive. Four relatives, positive for two antibodies, subsequently developed type 1 diabetes. Life-Table analysis of first-degree relatives with autoantibodies indicated an 80% disease-free survival at 3.5 yr. HLA-DRB1 was found to be associated with the presence of ICA in both probands and relatives, whereas HLA-DPB1 was associated with autoantibody in relatives of type 1 diabetic probands. These results suggest that autoimmunity occurs in type 1 diabetes families of Mexican descent in similar frequencies to that of non-Hispanic, Caucasian families. The presence of autoantibodies appears to be regulated in part by HLA class II genes, even in the absence of overt diabetes.

Tags: Female; Male
Descriptors: *Autoantibodies--analysis--AN; *Diabetes Mellitus, Type 1 --immunology--IM; *Genes, MHC Class II; *Mexican Americans; Adolescent; Adult; Alleles; Child; Child, Preschool; Diabetes Mellitus, Type 1 --ethnology--EH; Diabetes Mellitus, Type 1--genetics--GE; Glutamate Decarboxylase--analysis--AN; Humans; Insulin--immunology--IM; Middle Aged; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
CAS Registry No.: 0 (Autoantibodies); 0 (islet cell antibody); 11061-68-0 (Insulin)
Enzyme No.: EC 4.1.1.15 (Glutamate Decarboxylase)
Record Date Created: 20011015
Record Date Completed: 20011101

7/9/4 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13405046 PMID: 11579968

Stiff-person syndrome associated with cerebellar ataxia and high glutamic acid decarboxylase antibody titer.

Kono S; Miyajima H; Sugimoto M; Suzuki Y; Takahashi Y; Hishida A

First Department of Medicine, Hamamatsu University School of Medicine.

Internal medicine (Tokyo, Japan) (Japan) Sep 2001, 40 (9) p968-71, ISSN 0918-2918--Print Journal Code: 9204241

Publishing Model Print

Document type: Case Reports; Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Glutamic acid decarboxylase (GAD) is the main target of humoral autoimmunity in patients with insulin-dependent diabetes mellitus (IDDM) and stiff-person syndrome. We reviewed the case of a 46-year-old woman who had cerebellar ataxia before getting stiff-person syndrome and IDDM with high anti-GAD autoantibody titers. This was a rare case in which there were both the clinical symptoms of stiff-person syndrome and cerebellar ataxia. In western blot analysis her serum reacted with 65-kDa proteins from rat cerebellum, cerebral cortex, and spinal cord. Autoantibodies to GAD may cause functional impairment of gamma-aminobutyric acid (GABA) neurons in the spinal cord as well as in the cerebellum. (9 Refs.)

Tags: Female

Descriptors: *Autoantibodies--blood--BL; *Cerebellar Ataxia --complications--CO; *Diabetes Mellitus, Type 1--complications--CO; *Glutamate Decarboxylase--immunology--IM; *Stiff-Person Syndrome --complications--CO; Blotting, Western; Cerebellar Ataxia--diagnosis--DI; Cerebellar Ataxia--enzymology--EN; Cerebellar Ataxia--immunology--IM; Diabetes Mellitus, Type 1--enzymology--EN; Diabetes Mellitus, Type 1 --immunology--IM; Electromyography; Humans; Magnetic Resonance Imaging; Middle Aged; Stiff-Person Syndrome--diagnosis--DI; Stiff-Person Syndrome --enzymology--EN; Stiff-Person Syndrome--immunology--IM

CAS Registry No.: 0 (Autoantibodies)

Enzyme No.: EC 4.1.1.15 (Glutamate Decarboxylase)

Record Date Created: 20011002

Record Date Completed: 20020327

7/9/5 (Item 5 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13389103 PMID: 11561476

Insulin autoantibodies: evidence of autoimmune disease among a group of Puerto Rican children with newly diagnosed type 1 diabetes mellitus.

Gonzalez de Pijem L; Nieves-Rivera F

Endocrinology Section, Department of Pediatrics, University of Puerto Rico, School of Medicine, San Juan, Puerto Rico. Ligonzalez@Pol.net

Puerto Rico health sciences journal (Puerto Rico) Jun 2001, 20 (2) p161-4, ISSN 0738-0658--Print Journal Code: 8303541

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Type 1 diabetes is a chronic disease caused by a cell-specific destruction of the insulin producing cells of the pancreas. Although Puerto Rico has the highest incidence of type 1 diabetes among Latin American countries, there is scanty data on the presence of antibodies against insulin producing cells. To this end, 20 children (8 males, 12 females), ages 1-15 years, admitted to the University Pediatric Hospital with type 1 diabetes de novo between November 2000 and April 2001 were prospectively studied to determine the presence of serum antibodies against Islet cells (ICA), glutamic acid decarboxylase (GAD-65) and insulin autoantibodies (IAA). IAA was found to be present in 45% of the subjects with 85% of positive rate in subjects under age 5. GAD-65 was present in 66% and ICA was present in 23% of the subjects. We found evidence of autoimmunity against islet cell surface and intracellular components among a cohort of Puerto Rican children with newly diagnosed type 1 diabetes. These findings compared favorably with reports from other ethnicities.

Tags: Female; Male

Descriptors: *Autoantibodies--blood--BL; *Autoimmune Diseases--immunology --IM; *Diabetes Mellitus, Type 1--immunology--IM; *Insulin--immunology--IM ; Adolescent; Autoimmune Diseases--blood--BL; Child; Child, Preschool; Diabetes Mellitus, Type 1--blood--BL; Humans; Infant; Prospective Studies; Puerto Rico

CAS Registry No.: 0 (Autoantibodies); 11061-68-0 (Insulin)

Record Date Created: 20010919

Record Date Completed: 20020503

7/9/6 (Item 6 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13379872 PMID: 11552003

Stiff person syndrome: quantification, specificity, and intrathecal synthesis of GAD65 antibodies.

Dalakas M C; Li M; Fujii M; Jacobowitz D M

Neuromuscular Diseases Section, National Institute of Neurological Diseases and Stroke, NIH, Bethesda, MD 20892-1382, USA. dalakasm@ninds.nih.gov

Neurology (United States) Sep 11 2001, 57 (5) p780-4, ISSN 0028-3878--Print Journal Code: 0401060

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

OBJECTIVE: To characterize the specificity of anti-GAD(65) antibodies in patients with stiff person syndrome (SPS), quantify antibody titers, and examine antibody production within the CNS. METHODS: The authors studied 18 patients with SPS and positive serum immunoreactivity to gamma-aminobutyric acid (GABA)-ergic neurons. The reactivity of serum and CSF to purified GAD antigen was examined by Western blots, and the anti-GAD(65) antibody titers in serum and CSF were quantified by ELISA and compared with 70 disease controls (49 with other autoimmune disorders and 11 with insulin-dependent diabetes mellitus). The intrathecal synthesis of anti-GAD(65) IgG was calculated, and the functional significance of the antibodies was examined by measuring the GABA levels in the CSF. RESULTS: The serum and CSF of all selected patients with SPS had high anti-GAD(65) titers (from 7.0 to 215 microg/mL in serum and from 92 to 2500 ng/mL in CSF) and immunoreacted strongly with recombinant GAD(65) on Western blots and with GABA-ergic neurons on rat cerebellum. Among controls, only the serum of eight patients with insulin-dependent diabetes mellitus had low anti-GAD(65) antibody titers (from 200 to 1760 ng/mL) but no reactivity to recombinant GAD(65). The CSF showed oligoclonal IgG bands in 10 (67%) of 15 patients and an increased anti-GAD(65)-specific IgG index in 11 (85%) of 13. The mean level of GABA in the CSF was lower in patients with SPS than in controls. CONCLUSIONS: In patients with SPS, there is marked intrathecal antibody response against neuronal GAD(65) epitopes, indicating a clonal B cell activation in the CNS. Anti-GAD(65) antibodies at high titers, when confirmed with immunoblots, are highly specific for SPS and appear to impair GABA synthesis.

Descriptors: *Antibody Specificity; *Autoantibodies--biosynthesis--BI; *Autoantibodies--cerebrospinal fluid--CF; *Glutamate Decarboxylase --cerebrospinal fluid--CF; *Glutamate Decarboxylase--immunology--IM; *Isoenzymes--cerebrospinal fluid--CF; *Isoenzymes--immunology--IM; *Stiff-Person Syndrome--cerebrospinal fluid--CF; *Stiff-Person Syndrome --immunology--IM; Animals; Autoantibodies--blood--BL; Cerebellum --metabolism--ME; Diabetes Mellitus, Type 1--blood--BL; Diabetes Mellitus, Type 1--cerebrospinal fluid--CF; Glutamate Decarboxylase--blood--BL; Humans ; Immunoglobulin G--blood--BL; Immunoglobulin G--cerebrospinal fluid--CF; Isoenzymes--blood--BL; Rats

CAS Registry No.: 0 (Autoantibodies); 0 (Immunoglobulin G); 0 (Isoenzymes)

Enzyme No.: EC 4.1.1.- (GAD65 enzyme); EC 4.1.1.15 (Glutamate Decarboxylase)

Record Date Created: 20010911
Record Date Completed: 20011018

7/9/7 (Item 7 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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13312199 PMID: 11466400

MHC class I-restricted determinants on the glutamic acid decarboxylase 65 molecule induce spontaneous CTL activity.

Quinn A; McInerney M F; Sercarz E E

Division of Immune Regulation, La Jolla Institute for Allergy and Immunology, 10355 Science Center Drive, San Diego, CA 92121, USA.

Journal of immunology (Baltimore, Md. - 1950) (United States) Aug 1 2001, 167 (3) p1748-57, ISSN 0022-1767--Print Journal Code: 2985117R

Contract/Grant No.: AI28419; AI; NIAID
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: AIM; INDEX MEDICUS; Toxbib

CD4(+) T cell responses to glutamic acid decarboxylase (GAD65) spontaneously arise in nonobese diabetic (NOD) mice before the onset of insulin-dependent diabetes mellitus (IDDM) and may be critical to the pathogenic process. However, since both CD4(+) and CD8(+) T cells are involved in autoimmune diabetes, we sought to determine whether GAD65-specific CD8(+) T cells were also present in prediabetic NOD mice and contribute to IDDM. To refine the analysis, putative K(d)-binding determinants that were proximal to previously described dominant Th determinants (206-220 and 524-543) were examined for their ability to elicit cytolytic activity in young NOD mice. Naive NOD spleen cells stimulated with GAD65 peptides 206-214 (p206) and 546-554 (p546) produced IFN-gamma and showed Ag-specific CTL responses against targets pulsed with homologous peptide. Conversely, several GAD peptides distal to the Th determinants, and control K(d)-binding peptides did not induce similar responses. Spontaneous CTL responses to p206 and p546 were mediated by CD8(+) T cells that are capable of lysing GAD65-expressing target cells, and p546-specific T cells transferred insulitis to NOD.scid mice. Young NOD mice pretreated with p206 and p546 showed reduced CTL responses to homologous peptides and a delay in the onset of IDDM. Thus, MHC class I-restricted responses to GAD65 may provide an inflammatory focus for the generation of islet-specific pathogenesis and beta cell destruction. This report reveals a potential therapeutic role for MHC class I-restricted peptides in treating autoimmune disease and revisits the notion that the CD4- and CD8-inducing determinants on some molecules may benefit from a proximal relationship.

Tags: Female

Descriptors: *Cytotoxicity, Immunologic--immunology--IM; *Epitopes, T-Lymphocyte--immunology--IM; *Glutamate Decarboxylase--immunology--IM; *H-2 Antigens--immunology--IM; *Immunodominant Epitopes--immunology--IM; *Isoenzymes--immunology--IM; *T-Lymphocytes, Cytotoxic--enzymology--EN; *T-Lymphocytes, Cytotoxic--immunology--IM; Administration, Intranasal; Aging--immunology--IM; Animals; Animals, Newborn; Animals, Suckling; CD8-Positive T-Lymphocytes--enzymology--EN; CD8-Positive T-Lymphocytes --immunology--IM; Cell Line; Cyclophosphamide--administration and dosage --AD; Cytotoxicity Tests, Immunologic; Diabetes Mellitus, Type 1 --immunology--IM; Diabetes Mellitus, Type 1--prevention and control--PC; Freund's Adjuvant--administration and dosage--AD; Glutamate Decarboxylase --administration and dosage--AD; Glutamate Decarboxylase--genetics--GE; Injections, Intraperitoneal; Isoenzymes--administration and dosage--AD; Isoenzymes--genetics--GE; Mice; Mice, Inbred BALB C; Mice, Inbred NOD; Mice, SCID; Peptide Fragments--administration and dosage--AD; Peptide Fragments--immunology--IM; Rats; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Spleen--cytology--CY; Spleen--immunology--IM; T-Lymphocyte Subsets--enzymology--EN; T-Lymphocyte Subsets--immunology--IM ; Transfection

CAS Registry No.: 0 (Epitopes, T-Lymphocyte); 0 (H-2 Antigens); 0 (H-2K(K) antigen); 0 (Immunodominant Epitopes); 0 (Isoenzymes); 0 (Peptide Fragments); 50-18-0 (Cyclophosphamide); 9007-81-2 (Freund's Adjuvant)

Enzyme No.: EC 4.1.1.- (GAD65 enzyme); EC 4.1.1.15 (Glutamate Decarboxylase)

Record Date Created: 20010723

Record Date Completed: 20011025

7/9/8 (Item 8 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

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13302674 PMID: 11456277

A patient with type 1 diabetes mellitus and cerebellar ataxia associated with high titer of circulating anti-glutamic acid decarboxylase antibodies.

Iwasaki H; Sato R; Shichiri M; Hirata Y

Department of Clinical and Molecular Endocrinology, Tokyo Medical and Dental University Graduate School, Japan.

Endocrine journal (Japan) Apr 2001, 48 (2) p261-8, ISSN 0918-8959--Print Journal Code: 9313485

Publishing Model Print

Document type: Case Reports; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

A 66-year-old Japanese woman presenting with recent onset of type 1 diabetes mellitus and cerebellar ataxia was admitted to our hospital. Physical examination on admission revealed coordinate disturbance due to cerebellar ataxia, and the laboratory examination showed marked hyperglycemia with ketosis and impaired insulin secretion. Anti-glutamic acid decarboxylase (GAD) antibodies in high titer were detected in patient's serum. Immunoblotting showed the patient's serum reacted with a 65 kDa protein in tissue extracts from rat pancreas and cerebellum, and immunohistochemical study produced positive immunostaining in the pancreatic islets of Langerhans, the axons of Purkinje cells and the nerve terminals in the granular layers of cerebellum of the rat. This is the first case presenting with concomitant type 1 diabetes and cerebellar ataxi associated with high titers of circulating anti-GAD antibodies which may play a critical role in the development of the diseases.

Tags: Male

Descriptors: *Autoantibodies--blood--BL; *Cerebellar Ataxia--immunology --IM; *Diabetes Mellitus, Type 1--immunology--IM; *Glutamate Decarboxylase --immunology--IM; Aged; Animals; Axons--enzymology--EN; Cerebellar Ataxia --complications--CO; Cerebellum--enzymology--EN; Diabetes Mellitus, Type 1 --complications--CO; Humans; Immunoblotting; Immunohistochemistry; Isoenzymes--immunology--IM; Pancreas--enzymology--EN; Purkinje Cells --ultrastructure--UL; Rats; Research Support, Non-U.S. Gov't

CAS Registry No.: 0 (Autoantibodies); 0 (Isoenzymes)

Enzyme No.: EC 4.1.1.- (GAD65 enzyme); EC 4.1.1.15 (Glutamate Decarboxylase)

Record Date Created: 20010717

Record Date Completed: 20011207

7/9/9 (Item 9 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

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13269562 PMID: 11418696

Therapeutic alteration of insulin-dependent diabetes mellitus progression by T cell tolerance to glutamic acid decarboxylase 65 peptides in vitro and in vivo.

Wilson S S; White T C; DeLuca D

Department of Microbiology and Immunology, University of Arizona, Tucson, AZ 85724, USA.

Journal of immunology (Baltimore, Md. - 1950) (United States) Jul 1 2001, 167 (1) p569-77, ISSN 0022-1767--Print Journal Code: 2985117R

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

We have reported previously that nonobese diabetic (NOD) fetal pancreas organ cultures lose the ability to produce insulin when maintained in contact with NOD fetal thymus organ cultures (FTOC). Initial studies indicated that exposure to glutamic acid decarboxylase (GAD65) peptides in utero resulted in delay or transient protection from insulin-dependent diabetes mellitus (IDDM) in NOD mice. We also found that exposure of young adult NOD mice to the same peptides could result in acceleration of the disease. To more closely examine the effects of early and late exposure to diabetogenic Ags on T cells, we applied peptides derived from GAD65 (GAD AA 246-266, 509-528, and 524-543), to our "in vitro IDDM" (ivIDDM) model. T cells derived from NOD FTOC primed during the latter stages of organ culture, when mature T cell phenotypes are present, had the ability to proliferate to GAD peptides. ivIDDM was exacerbated under these conditions, suggesting that GAD responsiveness correlates with the ivIDDM phenotype, and parallels the acceleration of IDDM we had seen in young adult NOD mice. When GAD peptides were present during the initiation of FTOC, GAD proliferative responses were inhibited, and ivIDDM was reduced. This result suggests that tolerance to GAD peptides may reduce the production of diabetogenic T cells or their capacity to respond, as suggested by the in utero therapies studied in NOD mice.

Tags: Female

Descriptors: *Diabetes Mellitus, Type 1--immunology--IM; *Diabetes Mellitus, Type 1--prevention and control--PC; *Glutamate Decarboxylase --administration and dosage--AD; *Glutamate Decarboxylase--immunology--IM; *Immune Tolerance--drug effects--DE; *Isoenzymes--administration and dosage --AD; *Isoenzymes--immunology--IM; *Peptide Fragments--administration and dosage--AD; *Peptide Fragments--immunology--IM; *T-Lymphocytes--immunology --IM; Adjuvants, Immunologic--pharmacology--PD; Amino Acid Sequence; Animals; Animals, Newborn--immunology--IM; Coculture Techniques; Diabetes Mellitus, Type 1--enzymology--EN; Diabetes Mellitus, Type 1--etiology--ET;

Disease Progression; Dose-Response Relationship, Immunologic; Fetus; Glutamate Decarboxylase--pharmacology--PD; Immunization Schedule; Injections, Intraperitoneal; Isoenzymes--pharmacology--PD; Lymphocyte Activation--drug effects--DE; Mice; Mice, Inbred NOD; Molecular Sequence Data; Organ Culture Techniques; Peptide Fragments--pharmacology--PD; Pregnancy; Research Support, Non-U.S. Gov't; T-Lymphocytes--drug effects --DE

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Isoenzymes); 0 (Peptide Fragments)

Enzyme No.: EC 4.1.1.- (GAD65 enzyme); EC 4.1.1.15 (Glutamate Decarboxylase)

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Establishment of an expression cloning system for CD4+ T cell epitopes.

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We previously reported an epitope presenting vector, pCI, a derivative of a human invariant chain (Ii) expression vector, in which the class II associated invariant chain peptide (CLIP, Ii p89-101) could be substituted with antigenic peptides. In the current study, we used this vector to develop a new expression cloning system to identify CD4+ T cell epitopes. We inserted double-stranded oligo DNAs of randomized sequences into this vector and prepared an epitope-presenting library which loads randomized 13-mer peptides onto HLA class II molecules coexpressed in COS-7 cells. Utilizing this library, we isolated a cross-reactive epitope recognized by a glutamic acid decarboxylase (GAD) 65-autoreactive T cell clone established from a patient with insulin-dependent diabetes mellitus. Although the newly identified epitope (PVQLSNQWHVVGATF) was far different from the original epitope, GAD65 p116-128 (NILLQYVVKSFDR), it did have the capacity to stimulate the T cell clone comparable to that of the original GAD epitope. Our system may be applicable not only for identifying of cross-reactive epitopes for CD4+ T cells of known specificity, but also for detection of epitopes stimulatory for CD4+ T cells the epitopes of which are unknown. Copyright 2001 Academic Press.

Descriptors: *CD4-Positive T-Lymphocytes--immunology--IM; *Epitopes --genetics--GE; *Glutamate Decarboxylase--immunology--IM; *Isoenzymes --immunology--IM; Amino Acid Sequence; Antigens, Differentiation, B-Lymphocyte--immunology--IM; Base Sequence; Cloning, Molecular; Cross Reactions; Diabetes Mellitus--immunology--IM; Epitopes--immunology--IM; Genetic Vectors; Histocompatibility Antigens Class II--immunology--IM; Humans; Molecular Sequence Data; Peptide Library; Research Support, Non-U.S. Gov't

CAS Registry No.: 0 (Antigens, Differentiation, B-Lymphocyte); 0 (Epitopes); 0 (Genetic Vectors); 0 (Histocompatibility Antigens Class II); 0 (Isoenzymes); 0 (Peptide Library); 0 (invariant chain)

Enzyme No.: EC 4.1.1.- (GAD65 enzyme); EC 4.1.1.15 (Glutamate